REMARKS

Claims 1–28 are pending in the present application. Claims 2, 4, 6, 7, 10-13, 19-22 and 26-28 are canceled herein without prejudice. Claims 1, 3, 5, 8, 9, 14-18 and 23-25 are amended herein for clarity to more particularly define the invention. Support for these amendments is found in the language of the original claims and throughout the specification, as set forth below. The specification is amended herein to address the issues raised by the Examiner, as described herein, to reference Figure 10 in the specification and to correct various inadvertent typographical errors. No new matter is added by these amendments and their entry and examination are respectfully requested. In light of these amendments and the following remarks, applicants request reconsideration and allowance of the pending claims.

I. Specification Informalities

A. The Office Action states that Figure 5 on page 5 should recite Figures 5A and 5B to be consistent with the drawings.

The specification is amended herein as proposed by the Examiner to recite "Figures 5A and 5B." Thus, this objection has been overcome and applicants respectfully request its withdrawal.

B. The Office Action states that the use of trademarks in the application is noted and that such usage should be according to the proper format for reciting a trademark in a patent application.

The specification is amended herein to recite trademarks listed on pages 30 and 31 in the substitute specification in the proper format. Applicants note however, that the Examiner appears to list "Immunex" and "Invitrogen" as trademarks, when in fact, these are names of companies. Thus, no amendments were made to the paragraph on page

24 of the substitute specification where these terms are mentioned. Thus, this objection has been overcome and applicants respectfully request its withdrawal.

C. The Office Action states that the address of the American Type Culture Collection (ATCC) is incorrect as listed on page 21 of the substitute specification.

The substitute specification is amended herein to reflect the new address of the ATCC. Thus, this objection has been overcome and applicants respectfully request its withdrawal.

II. Rejection under 35 U.S.C. § 101

The Office Action states that claims 9, 10, 14 and 15 are rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter, on the basis that these claims as written do not sufficiently distinguish over nucleic acids or oligonucleotides as they exist naturally. The Examiner suggests that these claims be amended to recite the term "isolated" to overcome this rejection.

Claim 10 is canceled herein without prejudice, thereby mooting this rejection as it pertains to this claim. Claim 9 as presented herein recites a cell containing the expression vector of claim 8. Claim 9 depends from claim 8, which recites an expression vector comprising the polynucleotide according to claim 1 and claim 1 recites an isolated polynucleotide. Thus, by virtue of these dependencies, the cell of claim 9 comprises an isolated polynucleotide, thereby distinguishing the cell of claim 9 from a cell as it exists naturally. Thus, claim 9 as pending herein is not directed to non-statutory subject matter and applicants respectfully request that this rejection be withdrawn.

Furthermore, claim 14 recites an antisense oligonucleotide complementary to the polynucleotide of claim 1 and having a length sufficient to hybridize thereto under

physiological conditions and claim 15 recites a DNA encoding the antisense oligonucleotide of claim 14. As noted above, claim 1 recites an isolated polynucleotide and claims 14 and 15 include all of the limitations of claim 1, thereby distinguishing the nucleic acids claimed therein from non-statutory subject matter. However, in order to expedite prosecution of the pending claims to issue, claims 14 and 15 are amended herein to recite an isolated antisense oligonucleotide and an isolated DNA, respectively. Thus, this rejection has been overcome and applicants respectfully request its withdrawal.

III. Rejection under 35 U.S.C. § 112, first paragraph

The Office Action states that claims 23-25 and 28 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement.

Claims 23, 24 and 25 as presented herein recite a composition comprising the polynucleotide of claim 1 in a pharmaceutically acceptable carrier; the composition according to Claim 23 wherein the polynucleotide has the nucleotide sequence of SEQ ID NO:1; and a composition comprising the expression vector of claim 8 in a pharmaceutically acceptable carrier, respectively, thereby providing enabling embodiments of these claims, as noted by the Examiner. Claim 28 is canceled herein without prejudice, thereby mooting this rejection as it pertains to this claim. Thus, this rejection has been overcome and applicants respectfully request its withdrawal.

IV. Rejection under 35 U.S.C. § 112, second paragraph

The Office Action states that claims 1-3, 5, 8-10, 14-18, 23-25 and 28 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. The Examiner itemizes these rejections as items (a) through (t) in the Office Action and each of these rejections is addressed as follows in this format.

(a) Claim 1 is amended herein to recite the full terminology of the abbreviation "DsrA," thereby addressing this rejection as it pertains to claims 1-3, 5, 10 , 17 and 18.

(b) Claim 1 is amended herein to recite the stringency conditions as claimed therein, as supported on page 13, lines 19-21, of the substitute specification.

(c) Claim 2 is canceled herein without prejudice and claim 5 is amended herein to recite "The" instead of "A."

(d) Claims 8, 14 and 23 are amended herein to recite "the" instead of "a."

(e) Claims 3 and 5 are amended herein to recite "of" instead of "given herein as."

(f) Claim 9 is amended herein to recite "the expression vector of claim 8." Claim 10 is canceled herein without prejudice.

(g) Claim 25 is amended herein to recite "the expression vector of claim 8."

(h) Claim 10 is canceled herein without prejudice.

(i) Claims 15 and 16 are amended herein to recite "the antisense oligonucleotide of claim 14."

(j) Support for the term "fragment" as it is used in claim 17 is supported in the specification, for example, on page 11, lines 4-7, wherein it is stated that "'[f]ragments' are those nucleic acid sequences which are greater than 60 nucleotides than in length, and most preferably includes fragments that are at least 100 nucleotides or at least 1000 nucleotides, and at least 10,000 nucleotides in length." Thus, the term fragment

as used herein is definite and clear and the metes and bounds of a fragment of this invention can be readily determined by one of ordinary skill in the art.

(k) Claim 15 is clear and definite in its recitation of "DNA encoding the antisense oligonucleotide of claim 14," on the basis that this language is conventional in the art for describing antisense oligonucleotides and their sources. Specifically, in order to produce an antisense nucleic acid (other than by synthetic chemistry methods), the antisense oligonucleotide is generally encoded by a genetic construct such as an expression vector. It is well-known in the art that not all nucleic acids or RNAs encode polypeptides. A few examples of non-translated nucleic acids include antisense nucleic acids, RNAi, "guide" nucleic acids, snRNA, ribosomal RNA, *etc.*

Applicants are enclosing herewith two abstracts that explicitly describe expression vectors "encoding" antisense oligonucleotides (Mautino et al., "Inhibition of HIV-1 replication by novel lentiviral vectors expressing transdominant Rev and HIV-1 env antisense" *Gene Ther.* **9**:421-31 (2002); Weiss et al., "Antisense strategies in neurobiology" *Neurochemistry International* **31**:321-48 (1997)).

(l, m, n and o) Claim 18 as presented herein recites a method for detecting a polynucleotide which encodes DsrA in a biological sample, comprising: (a) contacting the complete complement of the polynucleotide sequence-selected from the group consisting of **SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15,** and **SEQ ID NO:17** with the biological sample under conditions whereby a nucleic acid hybridization complex can form if a polynucleotide which encodes DsrA is present in the biological sample; and (b) detecting the hybridization complex, whereby the presence of the hybridization complex detects the presence of the polynucleotide which encodes DsrA in the biological sample. Thus, claim 18 is clear and definite and recites proper antecedent basis for the terms recited therein.

(p and q) Claim 24 is amended herein to recite the composition according to claim 23 wherein the polynucleotide has the nucleotide sequence of SEQ ID NO:1

(r and s) Claim 28 is canceled herein without prejudice, thereby mooting this rejection as it pertains to this claim.

(t) As noted above, claim 1 as presented herein is clear and definite in its recitation and therefore, dependent claims 2, 3, 5, 8, 9, 14-18, 23-25 and 28 are clear and definite.

V. Rejection under 35 U.S.C. § 102(b)

The Office Action states that claims 1, 2, 8-10 and 14-16 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Skurnik et al.

Claim 1 as presented herein recites an isolated polynucleotide encoding a full length ducreyi serum resistance A (DsrA) protein, the polynucleotide selected from the group consisting of: (a) DNA having the nucleotide sequence of **SEQ ID NO:1**; (b) DNA having the nucleotide sequence selected from the group consisting of **SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15,** and **SEQ ID NO:17;** (c) polynucleotides that hybridize to DNA of (a) or (b) above under stringent conditions as exemplified by a wash stringency of 50% Formamide with 5x Denhardt's solution, 0.5% SDS and 1x SSPE at 42°C and which encode a full length DsrA; and (d) polynucleotides that differ from the DNA of (a) or (b) or (c) above due to the degeneracy of the genetic code and that encode a full length DsrA. Skurnik et al. does not disclose the polynucleotide of claim 1 as presented herein. Therefore, Skurnik et al. does not anticipate claim 1 or any claim dependent therefrom. Thus, this rejection has been overcome and applicants respectfully request its withdrawal.

No fee is believed due with this response. However, the Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

Respectfully submitted,

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1: Neurochem Int. 1997 Sep;31(3):321-48.
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Antisense strategies in neurobiology.

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The use of antisense oligodeoxynucleotides, targeted to the transcripts encoding biologically active proteins in the nervous system, provides a novel and highly selective means to further our understanding of the function of these proteins. Recent studies of these agents also suggest the possibility of their being used therapeutically for a variety of diseases involving neuronal tissue. In this paper we review studies showing the in vitro and in vivo effects of antisense oligodeoxynucleotides as they relate to neurobiological functions. Particular attention is paid to the behavioral and biochemical effects of antisense oligodeoxynucleotides directed to the various subtypes of receptors for the neurotransmitter dopamine. An example is also provided showing the effects of a plasmid vector expressing an antisense RNA targeted to the calmodulin mRNAs in the PC12 pheochromocytoma cell line. The advantages of antisense oligodeoxynucleotides over traditional pharmacological treatments are assessed, and the advantages of using vectors encoding antisense RNA over the use of antisense oligodeoxynucleotides are also considered. We also describe the criteria that should be used in designing antisense oligodeoxynucleotides and several controls that should be employed to assure their specificity of action.

Publication Types:
- Review

PMID: 9246677 [PubMed - indexed for MEDLINE]

1: Gene Ther. 2002 Apr;9(7):421-31.

Inhibition of HIV-1 replication by novel lentiviral vectors expressing transdominant Rev and HIV-1 env antisense.

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Retroviral vectors expressing transdominant negative mutants of Rev (TdRev) inhibit HIV-1 replication by preventing the nuclear export of unspliced viral transcripts, thus inhibiting the synthesis of Gag-Pol, Env and reducing the levels of genomic RNA available for packaging. Due to these effective mechanisms of inhibition, production of HIV-1-based lentiviral vectors expressing TdRev has been difficult. Here we describe HIV-based vectors in which expression of TdRev is negatively regulated by Rev expression. In these vectors, we maintained the wild-type HIV-1 Tat/Rev exons and intron configuration and its mode of splicing regulation. The second Rev exon was mutated to encode TdRev. Inhibition of TdRev expression by Rev during vector production yields high titer vector preparations. A second vector containing an additional anti-HIV gene (env-antisense) was constructed by flipping a 1.2-kb env fragment contained within the Tat/TdRev intron. SupT1 cells and primary CD4+ lymphocytes transduced with these vectors inhibit HIV-1 replication and show a preferential advantage for survival. Although these vectors are poorly mobilized to secondary target cells by wild-type HIV-1, they reduce the infectivity of the wild-type virions escaping inhibition.

PMID: 11938457 [PubMed - indexed for MEDLINE]